REMARKS

The only issues outstanding in the office action mailed March 19, 2009, are the rejections under 35 U.S.C. 112. Reconsideration of these issues, in view of the following discussion, is respectfully requested. It is submitted that, as no art has been cited currently, the following discussion places the claims in condition for allowance.

Rejection Under 35 U.S.C. 112, first paragraph

Solely claim 21 has been rejected under 35 U.S.C. 112, first paragraph. It is argued, at page 2-9 of the office action that the specification does not provide enablement for the treatment of asthma. Applicants respectfully disagree with this analysis. At the outset, it is noted that claim 31, reciting a method of inhibiting proliferation of T cells, and claim 32, reciting a method of inhibiting a cytokine production in human peripheral blood monocytes, are not subject to this rejection and, in the previous office action, were indicated to be enabled. The action of the present compounds, as PDE IV inhibitors, has been shown to be effective in the treatment of asthma, as noted in the present specification. See, for example, EP 77 92 91. However, at page 3, the office action appears to advance the argument that the treatment of asthma is not enabled because asthma has various varieties, some of which may be difficult to treat. This supposition, alone, is insufficient to support an enablement requirement. Indeed, the real concern of the office action, as expressed at page 7, appears to be that various prior asthma treatments have undesirable side effects and, thus, have not made it through clinical trials before the FDA. However, such concern with FDA approval is misplaced, and not the provinence of the patent office. The fact that various *prior* asthma treatments have not received commercial approval is simply not relevant.

Other than the articles cited in the office action indicating that certain prior art treatments failed to receive FDA approval, the office action offers no "reasons or evidence" why the *compounds of the claims* would not be effective to treat asthma. It is submitted that, in the absence of such reasons or evidence, there is no basis to doubt enablement of the present method claim 21. It is well established that an unsupported suggestion that reactants within a class defined by claims in a typical method of use application would not work, or that such claims embrace inoperative members, is insufficient basis alone for rejecting the claims. See *Ex parte Janin*, 209 U.S.P.Q. 761 (POBA 1979). In fact, it is clear that recitations in an Applicants' specification *must* be taken by the PTO as an assertion that all compounds encompassed in the claims are operative in the invention, in the absence of reasons or evidence to the contrary. *In re*

Marzocchi, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971).

The first paragraph of 35 U.S.C §112 requires only *objective* enablement. Where a specification teaches the manner and process of making and using the invention, the specification *must* be taken as sufficient under §112, unless there is reason to doubt the truth of these statements. See *Marzocchi*, supra. Applicants' specification clearly enables one to make and use the disclosed compounds in the claimed methods, as evidenced from the disclosure at page 5 - 7 setting forth pharmaceutical formulations and dosages and the examples which also detail the production of pharmaceutical formulations.

On the one hand, it is submitted that the Examiner has not provided any such reasons or evidence to doubt the assertion of utility in the specification and, thus, the further steps of the analysis as set forth in *Marzocchi* are not reached. As clearly stated in *Marzocchi*, mere *breadth* of the claims does not, without more, result in non-enablement. As the court stated in *Marzocchi*, supra (emphasis in original):

> Turning specifically to the objections noted by the Board as indicated above, it appears that these comments indicate nothing more than a concern over the *breadth* of the disputed term. If we are correct, then the relevance of this concern escapes us. It has never been contended that Applicants, when they included the disputed terms in their specification, intended only to indicate a single compound. Accepting, therefore, that the term is a generic one, its recitation must be taken as an assertion by Applicants that all of the 'considerable number of compounds' which are included in the generic term would, as a class, be operative to produce the asserted enhancement of adhesion characteristics. The only relevant concern of the patent office under these circumstances should be over the *truth* of any such assertion. The first paragraph of §112 requires nothing more than *objective enablement*. How such a teaching is set forth, either by the use of illustrative examples or by broad term analogy, it is of no importance.

Thus, the concern expressed in the Office Action, apparently that the term "asthma" used in the claimed method is broad, does not provide the reasons or evidence necessary by *Marzocchi* to pass beyond the necessity merely for objective enablement.

Further, in this regard, it is important to note, as a matter of law, that it is not necessary for Applicants' *method* claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods,

are interpreted to be *per se* functional. See *In re Angstadt*, 190 U.S.P.Q. 214 (CCPA 1976) and *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (CCPA 1974). These cases state that, for method claims, inoperative embodiments are not encompassed therein and the only question is whether it would be undue experimentation for one of ordinary skill in the art to determine the scope of the claim. This issue is discussed more fully below.

It is submitted that the PTO has not furnished reasons or evidence why the objective enablement of the present specification fails. The discussion of *In re Wands*, taking up a substantial amount of the Office Action, does *not* provide the necessary reasons or evidence as to why utility is deficient, but instead is reached only in other circumstances, e.g., to assess "undue experimentation." However, since the present method claims do not encompass inoperative embodiments as a matter of law, this analysis will be addressed herein in order to show that it is not undue experimentation to determine the scope of method claim 21.

With respect to the nature of the invention, the unpredictability alleged at page 5 of the office action is not supported by the "evidence" provided later that certain compounds have not received FDA approval. Moreover, with respect to the breadth of the claims, it is important to note that a determination of undue experimentation must be considered on a *compound by compound* or *indication by indication* basis. The mere fact that a claim is broad does *not* mean that it is undue experimentation is required to determine enablement of the compounds therein, if it is not undue experimentation to determine enablement for *each* compound in the scope of the claim. See, for example, *In re Colianni*, 195 U.S.P.Q. 150 (CCPA 1977). One of ordinary skill in the art can easily determine, with the protocols given in the specification, whether a given compound has the utility stated. Thus, the mere fact that many compounds must be tested is not dispositive of lack of utility.

With respect to the guidance given by the instant specification, is submitted that the guidance is adequate, inasmuch as pharmaceutical formulation information is given, one of ordinary skill in the art can clearly prepare the compounds for administration, dosages are given and the pharmaceutical art is well developed and administration of a compound for a given indication is quite routine. Moreover, screening protocols for determining the efficacy of the compounds are set forth in the specification where it is indicated that the details of using a given compound can be determined by routine testing using a known protocol which is correlated with human activity, see page 93, as well as pages 5-6.

With respect to working examples, it is well established that working examples are *not* required to provide enablement. See, for example, *In re Borkowski*, 164 U.S.P.Q. 642 (CCPA

1970).

With respect to the state of the art, PDE inhibitors are well known to be implicated in signaling pathways which are instrumental in the etiology of disease.

In conclusion, it is submitted that the *Wands* factors clearly do not result in undue experimentation in order to determine whether a given indication and/or a compound is within the scope of the present claims. Thus, objective enablement is clearly present.

To the extent that the discussion of undue experimentation is intended to provide reasons or evidence why the statement of objective enablement in the specification would be doubted, it is apparent that such reasons or evidence are intended to be the existence of various side effects and/or the absence of an *absolute* assurance that asthma could be treated by inhibition of PDE IV isozyme. However, it is again submitted that the PTO oversteps its bounds, in apparently requiring such absolute assurance. The PTO is not the FDA, see *In re Anthony*, 414 F.2d 1383, 162 USPQ 594 (CCPA 1969).

Finally, it is submitted that, even if the discussion in the Office Action were to provide reasons or evidence to doubt the objective enablement, the well known utility of PDE IV inhibitors to treat asthma would counter such reasons or evidence. As additional evidence of enablement, applicants previously provided the following references:

1. EP 731, 099 B1 from which page 10 discusses the use of phosphodiesterase IV inhibitors for treatment and prevention of acute and chronic inflammation (asthma is an inflammation of the bronchial passages) and specifically mentions "all kinds of asthma."
2. An overview from the "Comparative Toxigenomics Database" indicating that rolipram has utility in the treatment of asthma;

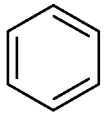
It is thus submitted to be amply clear that PDE IV inhibitors have art recognized utility as a class, and clearly, and that ample evidence of enablement of the present compounds has been provided. Accordingly, withdrawal of the rejection under 35 U.S.C. 112 is respectfully requested.

Rejections Under 35 U.S.C. 112, second paragraph

Claims 1-15 and 18 have been rejected under 35 U.S.C. 112, second paragraph as indefinite. Applicants respectfully disagree with this rejection.

At page 10 of the office action, it is argued that, in claim 1, the definition of R^3 and $R^{3'}$ lack proper valence of the nitrogen atom in the last two moieties. In fact, in a moiety like

"NCOA"R^7, NCOOA"R^7, NCOA or NCOOA" where the nitrogen formally lacks a valence, the skilled artisan (here: an organic chemist) clearly understands that the remaining bond is substituted by a hydrogen atom.

The same is e.g. true in all chemical formulae like benzene: 

where the skilled artisan knows that the missing valence on each carbon atom is substituted by hydrogen. It is further not understood why it is argued that an aromatic heterocyclic ring cannot be substituted by carbonyl oxygen, inasmuch as a double bond can be relocated to participate in the carbonyl bond, and still retain the heterocyclic character of the ring. Withdrawal of this rejection is accordingly respectfully requested.

It is submitted that the cancellation of claim 18 renders moot this rejection. Accordingly, withdrawal of the rejections under 35 U.S.C. 112 is respectfully requested, and it is submitted that all claims are in condition for allowance. Passage to issue is accordingly respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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